

**REMARKS**

At the outset, Applicant thanks the Examiners for the helpful interview held with him and Examiner Kemmerer on the morning of February 17, 2004. Applicant submits herewith the Associate Power of Attorney that the undersigned had taken to the interview.

Entry of this amendment is proper under 37 C.F.R. § 1.116, because the amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration, because the amendments amplify issues discussed throughout prosecution and during the interview; does not present any additional claims; and places the application in better form for an appeal should an appeal be necessary. The amendment and Declaration are necessary and were not earlier presented, because they are made in response to arguments raised in the final rejection as well as amplified during the interview with the Examiners. Entry of the amendment and Declaration under 37 C.F.R. § 1.132, reexamination, and further and favorable consideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.116 are thus respectfully requested.

**1. Status of the Claims**

As correctly noted in the Office Action Summary, claims 1-41, 43-52 and 54-58 have been canceled. Claims 42, 53, 59, and 60-72 stand pending.

Applicant has amended claims 42, 53, 59, 71 and 72. Claim 42 has been amended to recite a "neuronal progenitor cells and neuronal stem cells", and a composition comprising "an amount of growth hormone effective to propagate neuronal progenitor cells and neuronal stem cells *in vitro*." These changes were discussed during the interview. Support for the claim amendments can be found at least in the claims as originally filed.

Claim 59 has been amended to mirror the claim amendments in claim 42. Additionally, the claim now recites a patient in need of neuron propagation, and in step A an indication that the pharmaceutically effective amount is effective to propagate neuronal progenitor cells and neuronal stem cells. A superfluous recitation of "in need of neuron propagation regeneration" was removed from the claims. All the claims have been amended to italicize the term "*in vitro*".

In view of the claim amendments to claim 59, claim 53 was revised for purposes of clarity. Claim 71 removed a superfluous recitation of "in need of neuron regeneration", a comma was added to claim 72 after "Parkinson's disease" for clarity.

All the claims are supported at least by the original claims as filed. Consequently, no prohibited new matter is believed to have been introduced by entry of this amendment. Applicant reserves the right to file a continuation and/or divisional applications on any subject matter canceled by way of this or any amendment filed in the subject application.

During the interview, art discussed in paragraph 28 of the Office Action mailed June 10, 2003 (Paper No. 10) was clarified. Three references had been found during the Examiner's art search and were thus listed in the Office Action search. However, as discussed during the interview, the claims are free of these specific references, as these three references are not cited in a rejection against any claims.

Applicant notes with appreciation that the prior objections to the drawings, Oath and Declaration, and claims have been withdrawn. The Examiner has also withdrawn the rejections under 35 U.S.C. § 112, first paragraph, as set forth at pages 3-6, paragraph 6-12 of the June 10, 2003 Office Action (Paper No. 10), the rejection under § 112, second paragraph, and the rejection under § 102(a).

**2. Rejections Under 35 U.S.C. § 112, First Paragraph (Enablement)**

Claims 53, 59, and 62-72 stand rejected under § 112, first paragraph, as purportedly lacking enablement. During the interview with the Examiners, helpful recommendations regarding amendments to the claims were provided. These amendments have been introduced into claims 42 and 59. Additionally, Applicant now provides data, which was previously submitted to the Patent Office in Applicant's prior response, in the form of a Declaration by Peter Eriksson (the named inventor) pursuant to 37 C.F.R. § 1.132. The attached Declaration is being supplied, because of the assertion in the June 2003 Office Action that the example in the application is a non-specific test of cell proliferation. Specifically, BrdU was asserted to incorporate in a non-specific manner, and thus the observed result could be due to cell proliferation of glia and not to proliferation of neurons *per se*. The data provided herewith demonstrates that the growth hormone treatment results in an increase in neural stem proliferation, and not an increase in glia cell proliferation. As discussed during the interview with Examiners Kemmerer and Nichols, this data was deemed sufficient to overcome the Examiner's questions relating to enablement. In view of the Declaration and the amendments, Applicant asserts that the enablement rejection has been obviated. Accordingly, Applicant respectfully requests allowance of claims 53, 59, and 62-72.

**3. Rejection Under 35 U.S.C. § 102(b)**

**a. Rejection Under 35 U.S.C. § 102(b) as Anticipated by Almazon et al.**

Claims 42 and 60 stand rejected as purportedly anticipated by Almazon, (August 1985) "Epidermal Growth Factor in Bovine Growth Hormone Stimulate Differentiation in Milenation of Brain Cell Aggregates in Culture," *Developmental Brain Research* 21: 257-264.

Applicant respectfully traverses the rejection for the reasons previously of record, as well as those noted below. In the claimed methods, growth hormone is used to proliferate cells, and not to differentiate cells. The Almazon reference states

that all the changes appear to be correlated with an increased differentiation of the cells rather than with proliferation. See, Alamazon et al., at p. 262-263. The authors conclude that the presence of bovine growth hormone and EGF are associated with differentiation and not proliferation (*Id.*, at 263, last sentence). Accordingly, this reference would teach away from using growth hormone to proliferate cells, as its presence based on the study of these authors would indicate that they would differentiate cells.

Thus, Applicant respectfully requests withdrawal of the rejection under § 102(b) and allowance of the claims.

b. Rejection Under 35 U.S.C. § 102(b) as Anticipated by U.S. Patent No. 5,750,376

Claims 42, 60, and 61 stand rejected as purportedly anticipated by U.S. Patent No. 5,750,376 issued to Weiss et al. Applicant traverses the rejection for the reasons previously of record, as well as the arguments presented below.

As with the Alamazon reference, the cited patent does not teach the use of growth hormone for proliferation. Applicant directs the Examiners first to column 18, line 43 to column 20, line 56 of Weiss. This section discusses differentiation of neural stem cells. In the last paragraph of this section (*i.e.*, column 20, line 41 to 56), growth factors are listed that could be used to influence the differentiation of precursor cells *in vitro*. The list includes growth hormone. Thus, this reference teaches the use of growth hormone as a means of differentiating cells and not as a means of proliferating cells. Differentiating cells is contrary to the goals of the claimed methods, which is directed to proliferate or propagate cells that are neuronal progenitor cells and neuronal stem cells. Differentiation of these cells would be unwanted.

In fact, not only does the cited reference fail to recite all of the elements of the present invention, but it also fails to provide any suggestion of the elements of claimed invention. The presence of progenitor cells in the adult human brain was

first described in November 1998 (Eriksson et al. (1998) *Nature Medicine* 4(11); 1313-1317). At that time, very little was known about the regulation of stem/progenitor cell proliferation. Therefore, the data on growth hormone (GH) and its potential to induce proliferation in stem/progenitor cells in the adult brain which underlies the present invention was completely unexpected and unknown to those of skill in the art at the time the present application was filed. Further, the effect of GH on differentiated cells of the brain was essentially unknown at the time. GH was known to be present in several different brain tissues and, GH was known to affect psychological functions such as alertness, vitality and mood. However, the physiological mechanism by which GH mediated these effects was not known or understood (see Nyberg (1997) *Experimental Gerontology* 32:521-28).

Next, Applicant turns the Examiner's attention to column 15, line 63 to column 18, line 41, wherein the reference teaches *in vitro* proliferation of neural stem cells. Growth hormone is not one of the listed reagents that would serve to proliferate neural stem cells. Accordingly, when the reference is viewed as a whole and/or in light of what Almazon teaches, a skilled artisan would have been taught away from using growth hormone to proliferate cells.

As discussed in the last response provided by Applicant, "anticipation requires the presence in a single prior art disclosure of all elements of a claimed invention arranged as in the claims." Jamesbury Corp. v. Litton Industrial Products, Inc., 225 U.S.P.Q. 253, 256 (Fed. Cir. 1985). As both of the cited references teach the use of growth hormone for purposes of differentiating cells, Applicant submits that the claimed invention is neither taught nor suggested by the cited references and in fact teach away from the claimed invention. Accordingly, Applicant respectfully requests withdrawal of the rejection and allowance of the claims.

#### **4. Information Disclosure Statement**

Applicant noted that the considered IDS returned with the Office Action dated November 21, 2003, had three references stricken purportedly for the use of websites within the citation. Applicant is resubmitting another IDS for consideration

with the three cites. Applicant directs the Examiner's attention to M.P.E.P. §707.05(e) which provides 14 examples of how documents can be cited from the Internet. Applicants respectfully requests reconsideration of the cited references obtained from the internet. As discussed during the interview, as the references were previously submitted, no fee is required. However, as Applicant is submitting a new reference, Applicant is also submitting the requisite fee with the attached 1449 form and Information Disclosure Statement.

**CONCLUSION**

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited. In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney so that prosecution of this application may be expedited.

In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. 02-4800, including fees relating to a Notice of Appeal.

Respectfully submitted,  
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